REMARKS

Claims 1-9 were previously cancelled. Claims 10-20 were previously added. Accordingly, Claims 10-20 are pending. Accompanying this Amendment are two executed Declarations under 37 C.F.R. § 1.131.

Rejection under 35 U.S.C. 102(e) (U.S.P.N. 6,028,099)

Claims 10-17 and 19-20 have been rejected as being anticipated by U.S. Patent No. 6,028,099 ("the '099 patent") in view of the Cole Eye Institute article. (See Office Action page 2, paragraph 3.)

Independent Claim 10 recites methods of treating ocular disorders by administering an octreotide. Independent Claim 14 recites methods of treating an ocular disorder by *topically* administering a somatostatin analog in the form of an ophthalmic liquid preparation.

In contrast, the '099 patent discloses treating choroidal neovascularization (CNV) with the administration of an inhibitor of the protein tyrosine kinase pathway. (See col. 2, lines 15-18.) The Examiner points to the section of the patent which lists "various compounds that can be co-administered" with the inhibitor. Within this extensive list of compounds, the somatostatin analog SMS 201-995 is enumerated. (See col. 9, lines 14-24.)

The '099 patent was filed on March 13, 1998 and issued on February 22, 2000. The parent application of the present continuation application is U.S. Serial No. 09/258,240, filed on February 26, 1999. Thus, the parent application was filed before the '099 patent issued.

A 37 CFR § 1.131 Declaration executed by Dr. Robertus Wilhelmus Kuijpers was filed on April 25, 2005. Accompanying the present Amendment are two separate declarations pursuant to 37 C.F.R. §1.131 executed by the other two inventors (*i.e.*, Dr. Petrus Martinus van Hagen and Dr. Goitzen Seerp Baarsma). These three declarations establish that

conception of the present invention was achieved *prior to* the filing date of the '099 patent. Accordingly, the '099 patent is **not** available as a reference against the present application.

In particular, as can be seen in the declarations at paragraphs 3 and 4, the inventors treated a patient suffering from an ocular disorder associated with CNV with a somatostatin analog on October 16, 1996. As can be seen in the declarations at paragraphs 5 and 6, subsequent to October 16, 1996, there was a continuous diligence in reducing the invention to practice.

Since the present invention antedates the '099 patent, the '099 patent cannot be cited as a prior art reference. Accordingly the anticipation rejection is obviated.

However, even if the '099 patent could be cited (which Applicants strongly refute), the instant anticipation rejection of independent Claim 20 can be overcome for other reasons. Claim 20 recites methods of treating ocular disorders by "administering a pharmaceutical composition that **consists essentially of** octreotide..." The addition of an inhibitor of the protein tyrosine kinase pathway to a pharmaceutical composition that "consists essentially of" octreotide would materially affect the basic and novel characteristics of the pharmaceutical composition. For example, it is well known in the art that tyrosine kinase inhibitors have significant side effects. Thus, octreotide *without* a kinase inhibitor provides a safer clinical profile than octreotide *with* a kinase inhibitor.

It is *always* a principal goal in clinical medicine that side effects of medical treatments be minimized. The combination of octreotide with a drug with significant side effects would lead to a higher risk of side effects than when octreotide is used alone. Moreover, in the specification, it is shown that side effects were monitored and evaluated. See page 14, line 18, and page 15, line 26-27, of the specification. Thus, a minimization of side effects were *specifically* contemplated by the invention. Accordingly, excluding an agent which is known to have substantial side effects, such as the kinase inhibitors, was contemplated. The "consisting essentially of" language excludes such agents.

Moreover, **the Examiner has accepted the assertion that the addition of an inhibitor of the protein tyrosine kinase pathway** to a pharmaceutical composition that "consists essentially of" a somatostatin analogue **would materially affect the basic and novel characteristics** of the pharmaceutical composition in the counterpart application (U.S.S.N. 09/519,647). Accordingly, the same assertion should be accepted in the present application.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 18 recites a method of topically treating diabetic retinopathy with the administration of an octreotide in the form of an ophthalmic liquid preparation. The Examiner maintains the rejection of Claim 18 as not providing enablement for topical eye administration. (See Office Action page 3, paragraph 5.) The Examiner cites U.S. Patent No. 6,669,950 (hereinafter "the '950 patent") as discussing "problems associated with administering drugs to the posterior of the eye..."

In the April 1, 2005 Amendment, references were provided which demonstrate that topical compositions have been successfully used to treat posterior eye ailments, *e.g.*, glaucoma. In the present Office Action, the Examiner responds that "glaucoma [is] not a posterior eye disease."

The Applicants respectfully point out that the **'950 patent** (*i.e.*, the Examiner's cited reference) lists **glaucoma** as a **posterior eye ailment** at col. 1, line 23. (Note, Applicants have previously pointed out that the '950 patent lists glaucoma as a posterior eye ailment on page 6, last paragraph, of the April 1, 2005 Amendment.)

Additionally, according to M.PE.P. § 2164.04:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must be taken as being in compliance with the enablement requirement** of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. (Emphasis added.)

The instant specification teaches and describes the subject matter of Claim 18, *i.e.*, the treatment of diabetic retinopathy by the topical administration of octreotide. Thus, Claim 18 complies with the enablement requirement. Also, working examples are not necessary to comply with the enablement requirement. (See M.PE.P. § 2164.02.)

The '950 patent speaks only about disadvantages of periocular injections of a specific drug type, *i.e.*, angiogenesis inhibitors, not about periocular injections of all drug types. The patent does not speak of periocular injections in general. (See col. 1, lines 52-55, of the '950 patent.) It is improper to expand the teaching of the '950 patent to drugs other than angiogenesis inhibitors. In particular, the '950 patent does not teach anything about octreotide.

Moreover, as stated above, topical compositions have been successfully used to treat posterior eye ailments, *e.g.*, glaucoma. By way of example, Exhibits 1-5 were attached to the April 1, 2005 Amendment. Those exhibits are articles and a package insert demonstrating the use of several topically applied drugs to treat glaucoma. Thus, Applicants have provided evidence to demonstrate that drugs applied topically are used to treat posterior eye ailments.

Since the subject matter of Claim 18 complies with 35 U.S.C. 112, first paragraph, Applicants respectfully request withdrawal of the enablement rejection.

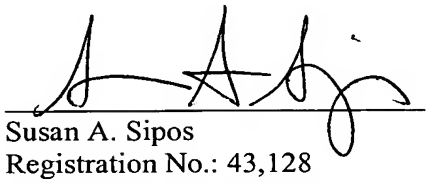
Obvious Type Double Patenting Rejection under 35 U.S.C. §101

The Examiner has also provisionally rejected the Claims 10-17 and 19-20 under the judicially created doctrine of obvious type double patenting in view of copending Application Serial No. 09/519,647. (See Office Action page 4, paragraph 7.)

Application Serial No. 09/519,647 has not yet been allowed. Once such application is allowed, Applicants will consider filing a terminal disclaimer which would ensure that the patent term of any patent that may issue from the present application would not extend beyond the term of any patent issued from Application Serial No. 09/519,647.

Applicants respectfully submit that the application, including Claims 10-20, is now in condition for allowance, which action is earnestly solicited. If resolution of any remaining issue is required prior to allowance of this application, it is respectfully requested that the Examiner contact Applicants' undersigned attorney at the telephone number provided below.

Respectfully submitted,



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